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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,144	09/26/2003	Lawrence Tamarkin	01994-0027 (42893/292447)	8073

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
10/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,144	TAMARKIN ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 1/3/2007.

Claims 27-35 are currently pending ad are addressed herein.

Election/Restrictions

Applicant's election without traverse of the combination of biologically active factors that is TNF-alpha and IL-12 in the reply filed on 1/3/2007 is acknowledged.

Claims 27-35 as they are drawn to the elected combination of factors are examined herein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 8/9/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

1. This application contains color photographs or drawings. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment

to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 27-35 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/21288 (cited by Applicants) as evidenced by Van Den Pol (Quarterly Journal of Experimental Physiol. 1984, 69:1-33) and NCBI MeSH, Tumor Necrosis Factor-alpha (www.ncbi.nlm.nih.gov/sites/entrez?db=mesh&cmd=search&term=tumor%20necrosis%20factor) and WO 95/249118.

The instant claims are drawn to a method for the delivery of more than one biologically-active factor (including treating cancer or an immune disease) comprising administering to a human or animal a composition comprising more than one biologically-active factor and a target molecule admixed with or bound to a colloidal metal wherein the more than one biologically active factor is TNF-alpha and IL-12 and wherein the colloidal metal is colloidal gold. It is

noted that at least on of the biologically active factors can be the targeting molecule (see claim 29).

WO 94/21288 teaches a composition and method that allows the administration of a biologically active factor to a human or animal without the normal toxic side effects by admixing the biologically active factor and a colloidal metal such as colloidal gold. WO 94/21288 teaches that the present invention can be used to treat a disease with a biologically active factor or a **combination of biologically active factors** (emphasis added), see Abstract. WO 94/21288 teaches that the present invention can be used to treat cancer or immune disease (e.g., see claim 19).

WO 94/21288 teaches that current therapies which comprise administering biologically-active factors to a human or animal are somewhat effective yet produce significant toxic side effects. Further, the toxic side effects limit the amount of antigen that may be administered, and therefore limit the efficacy of the therapy. Additionally, the toxicity of some biologically active factors precludes their use in such therapies. WO 94/21288 teaches that the combination of a colloidal metal with such biologically-active factors reduces toxicity while maintaining or increasing the therapeutic results thereby improving the efficacy as higher concentrations of biologically-active factors may be administered, or by allowing the use of **combinations of biologically-active factors** (emphasis added). WO 94/21288 teaches that the use of colloidal metals in combination with biologically-active factors therefore allows the use of higher concentrations of biologically-active factors or formerly unusable toxic substances, to be administered to humans or animals, see p.6, lines 23-31.

WO 94/21288 specifically teaches that IL-12 and Tumor Necrosis Factor as well as other biologically active factors can be used (e.g., see p.5, lines 17-28 and claim 4).

WO 94/21288 teaches that biologically active factor IL-1 mixed with colloidal gold retains its biological activity when administered *in vitro* to MCF-7 cells, see Example VI and Figure 2.

WO 94/21288 teaches that biologically active factor IL-6 efficiently binds colloidal gold, see Example VII.

Van Den Pol teaches that colloidal gold particles maintain a negative charge, and adsorb irreversibly to large protein molecules in solution. Gold particles will also adsorb to small proteins, but may not be stable and the gold may flocculate with time. Gold adsorbed to small proteins can be stabilized by the addition of a non-specific protein like bovine serum albumin, see p. 4, 4th para.

NCBI MeSH teaches that Tumor Necrosis Factor is another name for Tumor Necrosis Factor-alpha.

WO 95/249118 9/21/95 teaches that IL-12 known in vivo activities of IL-12 include increased survival in SCID mice, cure of leishmaniasis in susceptible strains of mice and suppresion of tumor growth. Thus, IL-12 is a chemotherapeutic agent.

Given that WO 94/21288 teaches IL-12 and TNF-alpha and combinations of these factors with colloidal gold and given Van Den Pol teaches that the negative charge of gold particles allows for protein binding, the product of the prior art comprises the same product as claimed in the instant invention, that is, a composition comprising IL-12 and TNF-alpha bound to a colloidal metal platform, thus the claimed product is anticipated because the product will

inherently be a targeted delivery composition comprising one or more effector molecules and one or more cell-specific targeting molecules bound to a colloidal metal platform; wherein the one or more effector molecules and the one or more cell specific targeting molecules are distinct molecules. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the biologically active factors IL-12 and TNF-alpha bound the colloidal gold, the product used in the claimed method appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product and methods of its use are different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Given that WO 94/21288 teaches using combinations of the biologically active factors of the instant invention, which include IL-12 and TNF-alpha, methods of delivery using the colloidal gold composition *in vitro* and *in vivo* to a cell specific or target site, and methods for reducing systemic toxicity of toxic biological active factors WO 94/21288 anticipates the instant claims.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 27-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33-35 and 45 of copending Application No. 09/189,657. Although the conflicting claims are not identical, they are not patentably distinct from each other because although the claims of the co-pending application are broader in scope and do not specifically claim the exact biological factors which are used and disease treated, using the disclosure of the co-pending application as a dictionary to define the biologically active factors which can be used, it is clear that the biological factors can be TNF-alpha and IL-12 and that the method can be used to treat cancer or an immune disease (e.g., see claims 22, 25).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner
Art Unit 1635